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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/287,500	04/07/1999	JOHN C. LEE	STK-1-DIV-3	6377

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EXAMINER

ROMEO, DAVID S

ART UNIT PAPER NUMBER

1647

DATE MAILED: 12/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action

Application No.

09/287,500

Applicant(s)

LEE ET AL.

Examiner

David S Romeo

Art Unit

1647

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 12 November 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

- a) ☒ The period for reply expires 4 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
- ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
- (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.
4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☒ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:


Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: 69,71,102,106,108-110 and 112-117.

Claim(s) withdrawn from consideration: 70,72,73 and 118-122.

8. ☐ The drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.
10. ☒ Other: Note the attached Notice of References Cited (PTO-892)


David S Romeo
Primary Examiner
Art Unit: 1647

Continuation of 2. NOTE: The amendment further restricts the scope of the claim, and would necessitate a further consideration of the other members of the Markush group of morphogenic proteins.

Continuation of 5. does NOT place the application in condition for allowance because: Applicants' arguments are directed to the newly proposed amended claims and that amendment has not been entered. Furthermore, Applicants' "obvious to try" argument does not speak to the obviousness of the combining a BMP and heparin. Furthermore, the teachings of the Wang (B, the paper mailed 01/16/2001), Kuberasampath (E, the paper mailed 01/16/2001) and Reddi (V, the paper mailed 11/17/2003) lead to a general expectation of greater than additive osteogenic effects when using mixtures of a BMP and IGF-I. Regarding the rejection of claims under 35 U.S.C. § 112, first paragraph, Applicants provide numerous references to show that AP activity correlates with the induction of bone in vivo. Although these references indicate that induction of alkaline phosphatase activity may be used to assess in vitro osteogenic activity, none of these references indicate that the synergistic enhancement of alkaline phosphatase activity is predictive of synergistic enhancement bone, cartilage, tendon/ligament, and neural tissue in vivo. It is further noted that Kang (Exhibit G, cited by Applicants) refers to a study by Li, which also suggests that BMP-9 is one of the most osteogenic BMPs in rat models of bone formation. However, Li also suggest that although previous studies have shown that alkaline phosphatase expression is a consistent in vitro osteogenic response seen in BMP-responsive cells and usually correlates with the ability of the various BMPs to induce bone formation in vivo, it may not accurately predict in vivo osteogenic potential (paragraph bridging pages 1738-1739). The only working example in the present specification is the induction of alkaline phosphate activity in FRC cells. There is nothing in the prior art of record or in the present specification that establishes a nexus between the induction of alkaline phosphate activity in FRC cells and the synergistic enhancement bone, cartilage, tendon/ligament, and neural tissue in vivo.